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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/776,479	02/02/2001	Robert L. Bratzler	C1037/7013 (HCL/MAT)	7139

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Helen C. Lockhart
c/o Wolf Greenfield & Sacks, P.C.
Federal Reserve Plaza
600 Atlantic Avenue
Boston, MA 02210

EXAMINER	
MINNIFIELD, NITA M	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 11/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/776,479	BRATZLER ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-19 and 37-52* is/are pending in the application.

4a) Of the above claim(s) *19,37,41,43,46 and 49-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-18,38-40,42,44,45,47,48 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) 5 sheets

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group I, claims 12-19 and 37-52 and species elections of CpG nucleic acid, down-regulator of IgE that itself an anti-Ig antibody or a fragment thereof and asthma medicament of bronchodilator/beta-2 agonist salbutamol, in the reply filed on August 18, 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 19, 37, 41, 43, 46 and 49-51 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on August 18, 2004.

3. Claims 12-18, 38-40, 42, 44, 45, 47, 48 and 52 will be examined in this pending application since they are directed to the elected invention (method of treating or preventing allergic asthma) and elected species (CpG nucleic acid, down-regulator of IgE that itself an anti-Ig antibody or a fragment thereof and asthma medicament of bronchodilator/beta-2 agonist salbutamol).

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. The use of trademarks has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

6. Claims 12-18, 38-40, 42, 44, 45, 47, 48 and 52 are objected to because of the following informalities: the recitation of non-elected subject matter should be deleted from the claims. Appropriate correction is required.

7. Claims 12-18, 38-40, 42, 44, 45, 47, 48 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 38-40, 42, 44, 45, 47, 48 and 52 are vague and indefinite in the recitation of "administering to the hypo-responsive subject an asthma/allergy medicament". The specification states and applicants' amendment state that hypo-responsive subjects have previously failed to respond to an asthma/allergy treatment, subjects that are at risk of not responding to such treatment, subjects that are refractory (i.e. does not respond or fails to respond) to an asthma/allergy medicament, and elderly subjects, provided that such subjects are not neonates. However, it is not clear which one of these Applicants intend for claim 38 for example. If the subject does not respond to asthma medicament or fails to respond to asthma medicament, why would one administer this asthma medicament in a sub-therapeutic amount or any other amount? With regard to claims 12-14 is there

a difference between a hypo-responsive subject and a subject who is refractory and one who is a non-responder? They would all appear to be the same. When the claims recite "asthma" does Applicants intend for this word to mean "allergic asthma", which is the invention that has been elected?

8. Claims 12-14 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Kline et al 1997 (J. Invest. Med., 45/7:298A) or Broide et al 1999 (Int. Arch. Allergy Immunol., 118:453-456).

The claims are directed to a method of administering an immunostimulatory nucleic acid (which can be CpG) to a hypo-responsive subject having allergic asthma or at risk of developing allergic asthma for treating or preventing allergic asthma. The claims also recite that the immunostimulatory nucleic acid has a modified backbone (phosphate modified backbone, phosphorothioate modified backbone). Additional claims also recite that asthma medicaments (immunomodulators, bronchodilator/beta-2 agonist, salbutamol) can be administered to the subject as well.

Kline et al 1997 (J. Invest. Med., 45/7:298A) discloses the administration of CpG, an immunostimulatory nucleic acid, to a subject. The prior art examined the effects of CpG in a murine model of asthma and found that CpG can prevent airway inflammatory upon allergen inhalation. Kline et al discloses that CpG may be useful in immunotherapy to prevent or treat asthma (abstract).

Broide et al 1999 discloses methods of administering an immunostimulatory nucleic acid, for example CpG, to a subject (abstract). Broide et al discloses the immunostimulatory nucleic acids induce Th1 cytokine production and inhibited Th2 cytokine production as well as eosinophilic inflammation when ISS was

administered before inhaled allergen challenge (abstract; materials and methods (p. 454; results, p. 454; Tables 1 and 2).

9. Claims 12-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Krieg et al (WO 98/18810).

Krieg et al discloses that CpG has a "...therapeutic utility in the treatment of asthma. Th2 cytokines, especially IL-4 and IL-5 are elevated in the airways of asthmatic subjects. These cytokines promote important aspects of the asthmatic inflammatory response, including IgE isotype switching, eosinophil chemotaxis and activation and mast cell growth. Th1 cytokines, especially IFN-γ and IL-12, can suppress the formation of Th2 clones and production of Th2 cytokines." (see pp. 65-66) Krieg et al discloses administering an immunostimulatory nucleic acid to a subject to treat or prevent allergies (p. 9; claims; p. 63). Krieg et al discloses that the ISS, CpG, has a modified phosphate backbone or phosphorothioate backbone modification (claims). Krieg et al discloses that the immunostimulatory nucleic acid is a T-rich nucleic acid (see claims). Krieg et al discloses that by redirecting a subject's immune response from Th2 to Th1, the claimed nucleic acid sequences (CpG) can be used to treat or prevent an asthmatic disorder. In addition, the claimed nucleic acid molecules can be administered to a subject in conjunction with a particular allergen as a type of desensitization therapy to treat or prevent the occurrence of an allergic reaction associated with an asthmatic disorder (see p. 10). Krieg et al discloses that an allergen refers to a substance that can induce an allergic or asthmatic response in a susceptible subject and list examples of such allergens (see p. 15). Krieg et al discloses that asthma refers to a disorder of the respiratory system characterized by inflammation, narrowing of the airways and

increased reactivity of the airways to inhaled agents. Asthma is frequently, though not exclusively associated with atopic or allergic symptoms (see p. 16).

10. Claims 12-18 are rejected under 35 U.S.C. 102(e) as being anticipated by Krieg et al (6124806 or 6239116), Davis et al (6406705) or Raz (6498148).

Krieg et al (6124806), for example, discloses administration of CpG, an immunostimulatory nucleic acid, to a subject to treat pulmonary disorders, such as asthma or environmentally induced airway disease (abstract; col. 3; example 2, col. 17; example 8, cols. 28-30; claims). Krieg et al disclose that the oligonucleotide, CpG, may have phosphate backbone modifications, phosphorothioate backbone modifications (col. 8) or that the oligonucleotide may be T-rich (col. 9). Krieg et al also discloses treatment of a subject having or at risk of having an acute decrement in air flow; this appears to be a subject at risk of asthma or allergic asthma (claims).

Krieg et al (6239116), for example, discloses administration of CpG, an immunostimulatory nucleic acid, to a subject (abstract; claims; cols. 45-46) to treat, prevent or ameliorate other disorders, which include asthmatic disorders or allergic reaction associated with an asthmatic disorder (cols. 6-7; col. 9-10; example 12, cols. 54-55). Krieg et al disclose that the oligonucleotide may have phosphate backbone modifications, phosphorothioate backbone modifications (col. 12) or that the oligonucleotide may be T-rich (col. 12).

11. Claims 12-18 are rejected under 35 U.S.C. 102(a) as being anticipated by Sur et al, 1999 (J. Immunology, 1999, 162/10:6284-6293).

Sur et al discloses that CpG can be used to treat asthma/allergic asthma (see materials and methods; p. 6289). Asthma is an inflammatory disease of the airways that is induced by Th2 cytokines and inhibited by Th1 cytokines. Despite a steady increase in the incidence, morbidity, and mortality from asthma, no current treatment can reduce or prevent asthma for a prolonged period of time (see abstract; p. 6284, cols. 1-2; p. 6292, col. 1).

12. With regard to Applicants' argument filed March 29, 2004 that none of the prior art discloses hypo-sensitive subjects, it is noted that Applicants' specification defines a hypo-responsive subject as subjects that have previously failed to respond to an asthma/allergy treatment, subjects that are at risk of not responding to such treatment, subjects that are refractory (i.e. does not respond or fails to respond) to an asthma/allergy medicament, and elderly subjects, provided that such subjects are not neonates. It would appear that the prior art discloses such subjects.

13. No claims are allowed.

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
October 31, 2004